Response to letter to the editor of Carcinogenesis by Li et al., 2020

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Keywords:	Helicobacter pylori; autoimmune pancreatitis; immunoglobulin G4-related disease; pancreatic cancer; apoptosis

Letter to the editor re: Li *et al*. (2020), 'The potential role of bacteria in pancreatic cancer: A systematic review'

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Dear Sir,

In their review Li et al. [1] focused on bacteria and particularly on *Helicobacter pylori* infection (*Hp*-I) involvement in pancreatic cancer pathophysiology by many molecular potential mechanisms.

Hp is the fundamental cause of gastric ulcer disease also associated with autoimmune pancreatitis (AIP) [2] and as a class I carcinogen may also be implicated, through molecular mimicry, in the pathophysiology of AIP and probably of pancreatic malignancy; this pathogen appears to be involved in AIP via induction of autoimmunity and apoptosis [3], and, apart from other molecular mechanisms some of which also mentioned by the authors [1,4] *Hp*-I may also contribute to pancreatic carcinogenesis by altered apoptotic pathways [4,5].

Specifically, relative data [6] identified that: a) peptide AIP1-7 showed homology with *Hp* plasminogen-binding protein (PBP) and with the enzyme biquitin-protein ligase E3 component n-recognin 2, expressed in pancreatic acinar cells; and b) the antibody against PBP was associated with AIP. *Hp* was found to bind plasminogen by *Hp* PBPs, enhancing its virulence [7]. These data appear to support our proposition [3,8] that *Hp* might trigger AIP through molecular mimicry and its increased virulence. Plasminogen binding and its conversion to plasmin is the only proteolytic activity of *Hp*, it may enhance tissue damage [7] and is involved in carcinogenesis; anti–PBP peptide antibody is present in patients with pancreatic cancer [6]. Besides, Guarneri et al. [9] found homology between human pancreatic autoantigen carbonic anhydrase II and α-carbonic anhydrase of *Hp,* a fundamental

enzyme for *Hp* survival and proliferation; the homologous segments contained the binding motif of the HLA molecule DRB1*0405 [9]. These data further strengthen our assumption that *Hp* infection can trigger AIP in genetically predisposed subjects and consequence pancreatic cancer.

In this regard several studies have proposed that the risk of pancreatic malignancy is high in patients with AIP [10]; IgG4-related disease is associated with cancer development especially during the first year after diagnosis, thereby signifying that active IgG4-related disease appears to be a strong risk factor for cancer development [11]; *Hp* a-carbonic anhydrase inhibitors may be introduced in the management of gastric ulcers and cancer [12]; pancreatic CAII-expressing cells give rise to new islet and acinar cells following birth and injury which may arise pancreatic malignancy from the uncontrolled growth of progenitor/stem cells [13]; bone marrow-derived stem cells (BMDSCs) are involved in the development and/or progression of pancreatic cancer [14]; and *Hp*-I by recruiting BMDSCs may facilitate cancer development and progression in animal models and humans [15,16].

Therefore, *Hp* eradication may also positive influence AIP patients by ameliorating the autoimmune sequelae and subsequent development of pancreatic cancer, and thus further studies are needed.

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